REMARKS

Claims 1-85 and 87 were pending in the application. Claims 2, 6-25, 46 and 47 have been cancelled without prejudice and claims 1, 3-5, 48-50, 67, 69, 70, 81 and 82 have been amended. Therefore, claims 1, 3-5, 26-45, 48-85 and 87 are currently pending.

No new matter has been added. Claim 1 has been amended to be directed to a method of treating or preventing malaria in a subject by administering a substituted tetracycline of formula I where R^7 is a malaria interacting moiety and R^9 is hydrogen. Claim 3 has been amended to provide proper dependency. Claims 4 and 5 have been amended to be directed to a method of treating or preventing malaria in a subject with a substituted tetracycline compound of formula I in which R^5, R^6, and $R^{6'}$ are each hydrogen or R^5 is hydroxy or a prodrug moiety, R^6 is methyl and $R^{6'}$ is hydrogen, respectively. Claims 48 and 49 have been amended to specify that the substituted tetracycline of claim 1 is a 7-substituted tetracycline compound. Claims 48 and 49 have been further amended to provide proper dependencies and correct a minor typographical error. Claim 50 has been amended to provide proper dependency. Claim 67 has been amended to be directed to a method of increasing the antimalarial activity of an antimalarial compound by administering a substituted tetracycline compound of formula I in which R^7 is a malaria interacting moiety and R^9 is hydrogen. Claim 69 has been amended to be directed to a method for preventing malaria in a mammal by administering a substituted tetracycline of formula I in which R^7 is a malaria interacting moiety and R^9 is hydrogen. Claim 70 has been amended to specify that the substituted tetracycline of claim 69 is a 7-substituted tetracycline compound and to correct a minor typographical error. Claim 81 has been amended to be directed to a pharmaceutical composition comprising an effective amount of a substituted tetracycline compound of formula I to treat malaria in a mammal and a pharmaceutically acceptable carrier where R^7 in formula I is a malaria interacting moiety and R^9 in formula I is hydrogen. Claim 82 has been amended to specify that the substituted tetracycline of claim 81 is a 7-substituted tetracycline compound and to correct a minor typographical error.

Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of and/or amendments to the claims is being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The cancellation of and/or amendments to the claims is not related to any issues of patentability.

Examiner's Remarks on Response to Restriction Requirement

The Examiner asserts that the claimed invention is too broad and that a "detailed search on databases were not possible." Further, the Examiner has requested that Applicant limit the claims to a subgenus of the elected species.

While in no way acquiescing to the Examiner's characterization of the claims and solely in an effort to expedite prosecution, Applicants have amended independent claims 1, 67, 69 and 81 to be directed to methods and compositions for treating malaria with substituted tetracycline compounds of formula I in which R^7 is a malaria interacting moiety and R^9 is hydrogen.

The Examiner further requests that Applicants provide the references and/or reasons for the disclaimer in claim 1. Applicants note that claim 1, as amended, no longer recites the disclaimer.

Information Disclosure Statement

The Examiner has requested that Applicants "tell the relevancy of the cited references in the IDS."

In accordance with 37 C.F.R. 1.97 and 1.98, Applicants made of record the references listed on the SB/08 forms filed on October 28, 2004 and June 6, 2006. Applicants cited these references to meet their duty of disclosure, in accordance with 37 C.F.R. 1.56.

According to MPEP 609, the Examiner has an obligation to consider the information once Applicants have filed the Information Disclosure Statements in accordance with 37 C.F.R. 1.97 and 1.98. Therefore, Applicants request that the Examiner consider the documents cited on the SB/08 forms.

Co-Pending Applications

The Examiner has requested that Applicants bring to the attention of the Examiner "information within their knowledge as to other co-pending United States applications..." Applicants respectfully direct the Examiner's attention to the list of the co-pending applications provided in the Information Disclosure Statement filed with the Office on June 6, 2006.

Rejection of Claims 1-85 and 87 under 35 U.S.C. §112, second paragraph

Claims 1-85 and 87 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Specifically, the Examiner requests clarification of the term "malaria interacting moiety."

Applicants respectfully submit that the term "malaria interacting moiety" is defined in the specification at page 8, lines 18-27 as "a moiety which allows the substituted tetracycline compound of the invention to perform its intended function, *e.g.*, treat or prevent malaria" and that the malaria interacting moiety "may interact with the malaria parasite or allow other portions of the tetracycline molecule to interact with the parasite" and "may allow the molecule to treat malaria by affecting the way the tetracycline compound interacts with the malaria parasite, the subject, or other microbes...[and] may alter the tetracycline compounds' properties such that the resulting compound is...non-antibacterial." Moreover, the specification, at pages 8, line 28 through page 12, lines 12, describes in detail the possible chemical structures of the malaria interacting moiety. Accordingly, Applicants respectfully submit that a skilled artisan in possession of the specification would readily be able to determine the meaning of the term "malaria interacting moiety." Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 1-85 and 87 under 35 U.S.C. §112, first paragraph

Claims 1-85 and 87 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner asserts that the "[c]laimed invention is too broad that [a] detailed and thorough search on databases were not possible." The Examiner further asserts that "[t]here are no examples or guidance showing that Applicants were in possession of all of the methods and compositions as the time of effective filing date."

Applicants respectfully traverse. However, to expedite prosecution, Applicants have amended independent claims 1, 67, 69 and 81 to be directed to methods and compositions for treating malaria with substituted tetracycline compounds of formula I in which R^7 is a malaria interacting moiety and R^9 is hydrogen. Accordingly, The Examiner's rejection of the claims under 35 U.S.C. § 112, first paragraph, does not pertain to the currently pending claims, because the currently claimed subject matter is described in the specification in a manner which would enable one of ordinary skill in the art to use the invention for at least the following reasons.

As described above, the term "malaria interacting moiety" is described in the specification at pages 8, line 18 through page 12, line 12. In addition, the specification, at least at page 81, line 1

through page 86, line 5 provides general synthetic methods for the synthesis of the substituted tetracycline compounds of the invention. Further, Applicants respectfully submit that the Examples in the specification fully support the claimed methods and compositions. Specifically, Example 1 describes the synthesis of representative examples of tetracycline compounds substituted at the 7-position with a malaria interacting moiety. Moreover, Example 3 provides detailed experimental methods for assessing the anti-malarial activity and data for approximately 250 substituted tetracycline compounds *in vitro*. Example 4 provides detailed experimental methods for assessing the anti-malarial activity for substituted tetracycline compounds *in vivo*.

Accordingly, Applicants respectfully submit that the specification describes the claimed invention in sufficient detail that a skilled artisan would conclude that Applicants had possession of the claimed invention at the time the application was filed. Based at least on the foregoing, Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 1-85 and 87 under 35 U.S.C. §112, first paragraph

Claims 1-85 and 87 are rejected under 35 U.S.C. §112, first paragraph, for not being enabled. Specifically, the Examiner asserts that "the specification, while being enabling for certain compounds and methods, does not reasonably provide enablement for hundreds of thousand of compositions containing tetracycline compounds..." The Examiner further states that "Applicant is requested to let us know where is the example to use [the elected species] for the methods as claimed."

Applicants respectfully traverse. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404.

As described above, Applicants have amended independent claims 1, 67, 69 and 81 to be directed to methods and compositions for treating malaria with substituted tetracycline compounds

of formula I in which R^7 is a malaria interacting moiety and R^9 is hydrogen. Further, Applicants respectfully submit that the relative skill of those skilled in the art in relation to the subject matter is high. With regard to the amount of direction provided by Applicants and the existence of working examples, Applicants respectfully direct the Examiner's attention to the general synthetic methods described in the specification and to the Examples, which describe the synthesis of representative examples of tetracycline compounds substituted at the 7-position with a malaria interacting moiety and provide detailed experimental methods for assessing the anti-malarial activity of substituted tetracycline compounds *in vitro* and *in vivo*. Furthermore, Applicants provide *in vitro* data for approximately 250 tetracycline compounds in Table 2. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). Moreover, it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. 112, first paragraph. *See* MPEP 2164.01(c). Upon weighing these factors, Applicants respectfully submit that a skilled artisan in possession of the specification would be able to make and use the claimed invention without undue experimentation.

With regard to the elected species, support for the elected species can be found, for example, at least on page 125 of the specification as originally filed (Compound FV of Table 2). Support for using this compound for the methods of the invention can be found, for example, at least at page 7, line 5 through page 12, line 36 and in claims 49 and 50, as originally filed.

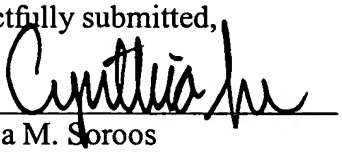
Based at least on the foregoing, Applicants respectfully request reconsideration and withdrawal of this rejection.

SUMMARY

In view of the amendments and remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Dated: February 26, 2007

Respectfully submitted,

By 

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